REMARKS

Introductory Comments

Claims 45-65 are pending in the application. Claims 49-62 are withdrawn as being drawn to non-elected inventions. Claims 3-5, 8, 45, and 46 are under active consideration.

Applicants note with appreciation the withdrawal of the previous rejection under 35 U.S.C. § 112, first paragraph.

Priority

The Office Action states that the present application is not entitled to the benefit of priority of provisional U.S. Application Serial No. 60/161,713 filed October 27, 1999 (Office Action, page 3). However, the provisional application does describe polynucleotides encoding NS3NS4NS5 fusion proteins (see, *e.g.*, page 9, lines 8-10). The reference of Cho only describes polynucleotides encoding fusion proteins containing HCV NS3, NS4, and NS5 polypeptides and not the claimed subject matter. Applicants need only show that they were in possession of as much of the invention as shown by the reference prior to its effective date (*In re Clarke*, 148 U.S.P.Q. 665 (CCPA 1966); *In re Stempel*, 113 U.S.P.Q. 77 (CCPA 1957)). Applicants are submitting herewith a copy of a Rule 131 Declaration filed in the parent application, USSN 09/698,874, which was effective in removing Cho as prior art. The Declaration establishes that Applicants had possession of constructs encoding NS345 fusions prior to March 1999. The Rule 131 Declaration submitted herewith removes Cho as a reference since it shows that applicants had in their possession fusion proteins as described in Cho prior to March 1999. For completeness, the rejection under 35 U.S.C. § 103(a) is addressed below.

35 U.S.C. § 103

A. Houghton '864 or Houghton '889 or Houghton '771

Claims 45-48 and 63-65 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Houghton et al. (U.S. Patent No. 5,683,864; hereinafter "Houghton '864") or Houghton et al. (U.S. Patent No. 6,312,889; hereinafter "Houghton '889") or Houghton et al.

(International Patent Publication No. WO 91/15771; hereinafter "Houghton '771"). Houghton '864, '889, and '771 are cited for teaching a method for making a fusion protein that comprises a region of the HCV core protein and at least one other HCV antigen selected from NS3, NS4, S, or NS5 (Office Action, page 4). The Office Action alleges that it would have been obvious for a person of ordinary skill in the art to make a polynucleotide encoding a fusion protein comprising full-length NS3, and NS4, NS5a, NS5b and core antigens, absent unexpected results (Office Action, page 4). Applicants respectfully traverse the rejection and the supporting remarks.

The decision by the Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007) reaffirmed the viability of the four factual inquiries underlying an obviousness analysis provided in *Graham v. John Deere*, 148 USPQ 459, 467 (U.S. 1966). These factors include: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary considerations. Moreover, the Supreme Court in *KSR* recognized that the "teaching, suggestion, or motivation" analysis provides a helpful insight in determining whether the claimed subject matter is obvious. This analysis is provided in MPEP 2142. In particular, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Additionally, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Both the teaching or suggestion to make the claimed combination, as well as the reasonable expectation of success, must be found in the prior art, not in applicant's disclosure. See, *e.g.*, *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Based on the foregoing, applicant respectfully submits the Office has failed to establish a *prima facie* case of obviousness.

Houghton '864, Houghton '889, and Houghton '771 pertain to immunoassays using polypeptide antigens for detection of antibodies in sera, not to nucleic acid immunization with polynucleotides encoding HCV antigens for eliciting an immune response, as in the instant application. Accordingly, the compositions described by Houghton '864 or Houghton '889 or Houghton '77 lack polynucleotides, as claimed, which would have no purpose in immunoassays. Similarly, the compositions of the cited references lack adjuvants (claims 64 and 65), which also

would have no purpose in immunoassays. Furthermore, Houghton '864, Houghton '889, and Houghton '771 fail to describe or suggest a fusion protein comprising a full length NS3 polypeptide, as recited in the claims. On the contrary, the references describe a fusion protein comprising an NS3 region derived from residues 1050-1640 (see Houghton '864 at col. 4, lines 21-23; Houghton '889 at col.4, lines 8-10; and Houghton '771 at page 6, lines 31-33). Therefore, Houghton '864, Houghton '889, and Houghton '771 fail to disclose or suggest the claimed polynucleotides.

For at least these reasons, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

B. Cho and Lagging or Geissler

Claims 45-48 and 63-65 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the reference of Cho et al. (Vaccine (1999) 17:1136-1144; hereinafter "Cho") in view of the reference of Lagging et al. (J. Virol. (1995) 69:5859-5863; hereinafter "Lagging") or Geissler et al. (J. Immunol. (1997) 159:5107-5113; hereinafter "Geissler"). Cho is cited for teaching a plasmid encoding a polyprotein fusion comprising NS3, NS4, and NS5 polypeptides, including NS5a and NS5b residues in the region from 1019 to 3010 (Office Action, page 4). Geissler and Lagging are cited for teaching that the HCV core antigen contains both T cell and B cell immunological epitopes that are able to induce significant T cell (CTL and cytokine) and B cell humoral responses (Office Action, page 5). The Office Action alleges:

> Therefore, it would have been obvious for any person [of] skill in the art to be motivated for making a DNA vaccine composition comprising the polynucleotide sequences encoding both HCV structural core and non-structural NS345 antigens that are approved to induce an optimal level of immune responses against each of the HCV antigens. (Office Action, page 5)

Applicants respectfully traverse the rejection and the supporting remarks.

As mentioned above, Applicants are submitting herewith a copy of a Rule 131 Declaration filed in the parent application, USSN 09/698,874, which was effective in removing Cho as prior art. In particular, the Declaration evidences that applicants had constructs

in-hand encoding NS345 fusions as described in Cho prior to Cho's publication date of March 1999. This date is less than one year prior to applicants' priority date of October 27, 1999. In order to remove Cho as a reference under Rule 131, applicants need only show that they were in possession of as much of the invention as shown by the reference prior to its effective date (*In re Clarke*, 148 U.S.P.Q. 665 (CCPA 1966); *In re Stempel*, 113 U.S.P.Q. 77 (CCPA 1957)). Thus, the Rule 131 Declaration submitted herewith removes Cho since it shows that applicants had in their possession fusion proteins as described in Cho prior to March 1999. Accordingly, Cho is not properly citable art and this basis for rejection has now been overcome.

Furthermore, the secondary references of Lagging and Geissler only describe vectors expressing the HCV core antigen and fail to describe or suggest combining the core polypeptide with any other HCV polypeptides. Therefore, neither Lagging or Geissler describe or suggest the claimed invention.

For at least these reasons, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

In light of the above remarks, applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at 650-493-3400.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

Please direct all further written communications regarding this application to:

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